(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 19 April 2001 (19.04.2001)

PCT

(10) International Publication Number WO 01/027158 A3

(51) International Patent Classification7: C12N 15/12, C07K 14/705, C12N 5/10, G01N 33/50, C12Q 1/68

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(21) International Application Number: PCT/US00/27582

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(22) International Filing Date: 6 October 2000 (06.10.2000)

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/158,615 60/184,809 8 October 1999 (08.10.1999) U 24 February 2000 (24.02.2000) U

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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Published:

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with international search report

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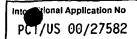
(88) Date of publication of the international search report: 26 September 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

43

(54) Title: OLFACTORY RECEPTOR SEQUENCES

(57) Abstract: The present invention provides polynucleotide sequences which encode polypeptides involved in olfactory sensation. The present invention also provides the polypeptides encoded by these polynucleotide sequences, vectors comprising these polynucleotide sequences and host cells transfected with these polynucleotide sequences. The present invention further provides for functional variants and homologues of these polynucleotide sequences and the polypeptides encoded by these polynucleotides. Libraries of polypeptides are also provided. Also included in the present invention is the use of these polypeptides and libraries of polypeptides in screening odorant molecules to determine the correspondence (scent representation, scent fingerprint or scent profile) between individual odorant receptors (the polypeptides) and particular odorant molecules. Also encompassed by the present invention is the use of the scent representation, scent fingerprint or scent profile to re-create and edit scents.



A. CLASS IPC 7	C12N15/12 C07K14/705 C12N5/	10 G01N33/50	C12Q1/68
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C. DOCUM	ENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the re	elevant passages	Relevant to claim No.
A	WETZEL CHRISTIAN H ET AL: "Speciand sensitivity of a human olfact receptor functionally expressed embryonic kidney 293 cells and place of socytes." JOURNAL OF NEUROSCIENCE, vol. 19, no. 17, pages 7426-743 XP002178954 ISSN: 0270-6474 cited in the application the whole document WO 95 18140 A (YEDA RES & DEV ; RAVIGALL (IL); BEN ARIE NISSIM (ID) 6 July 1995 (1995-07-06) pages 3,4,6; Figs 3 + 4	etory in human Kenopus 33,	
X Furth	er documents are fisted in the continuation of box C.	X Patent family members are	e listed in annex.
Special cat	egories of cited documents :		
"A" documer conside	nt defining the general state of the art which is not ared to be of particular relevance ocument but published on or after the international	 "T" later document published after to priority date and not in conficited to understand the princip invention "X" document of particular relevance 	ict with the application but le or theory underlying the
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	NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,	Holtorf, S	

In tional Application No PCT/US 00/27582

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	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	Delayant to object No.
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to daim No.
A	GLUSMAN GUSTAVO ET AL: "Sequence analysis in the olfactory receptor gene cluster on human chromosome 17: Recombinatorial events affecting receptor diversity." GENOMICS, vol. 37, no. 2, 1996, pages 147-160, XP002178955 ISSN: 0888-7543 the whole document & DATABASE EMBL SEQUENCE LIBRARY [Online] 22 July 1994 (1994-07-22)	
	CROWE M.L., PERRY B.N., CONNERTON I.F.: "olfactory receptor; OR17-40 gene" abstract	
A	BUETTNER JILL A ET AL: "Organization and evolution of olfactory receptor genes on human chromosome 11." GENOMICS, vol. 53, no. 1, 1 October 1998 (1998-10-01), pages 56-68, XP002178956 ISSN: 0888-7543 the whole document	
	TRASK B J ET AL: "Members of the olfactory receptor gene family are contained in large blocks of DNA duplicated polymorphically near the ends of human chromosomes" HUMAN MOLECULAR GENETICS, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 7, no. 1, January 1998 (1998-01), pages 13-26, XP002135641 ISSN: 0964-6906 the whole document	
	& DATABASE EMBL SEQUENCE LIBRARY [Online] 9 June 1996 (1996-06-09) TRASK, B.J., ET AL.: "Homo sapiens chromosome-19 36.3-kbp cosmid F7501, with 3 regions of similarity to olfactory receptor protein genes" accession no. L78442	
	KRAUTWURST D ET AL: "Identification of ligands for olfactory receptors by functional expression of a receptor library" CELL, CELL PRESS, CAMBRIDGE, NA, US, vol. 95, 25 June 1998 (1998-06-25), pages 917-926, XP002153217 ISSN: 0092-8674 cited in the application	
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Interplonal Application No PCT/US 00/27582

	A COMMENTS CONCIDENTS TO BE DELEVANT	101/03 00/2/302
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Category *	Citation of document, with indication, where appropriate, or the relevant passages	
A	WO 98 50081 A (ZHAO HAIQING ;FIRESTEIN STUART J (US)) 12 November 1998 (1998-11-12) cited in the application	
P,X	DATABASE EMBL SEQUENCE LIBRARY [Online] 14 June 2000 (2000-06-14) HEILIG R., ET AL.: "Human chromosome 14 DNA sequence BAC R-55G7 of library RPCI-11 from chromosome 14 of Homo sapiens (Human)" XP002178959 accession no. AL359218	1,4
T	GLUSMAN GUSTAVO ET AL: "Sequence, structure, and evolution of a complete human olfactory receptor gene cluster." GENOMICS., vol. 63, no. 2, 15 January 2000 (2000-01-15), pages 227-245, XP002178957 ISSN: 0888-7543 the whole document	
T	FUCHS TANIA ET AL: "The human olfactory subgenome: From sequence to structure and evolution." HUMAN GENETICS, vol. 108, no. 1, January 2001 (2001-01), pages 1-13, XP002178958 ISSN: 0340-6717	

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)	
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:	
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:	
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:	
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).	
Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)	.,
This International Searching Authority found multiple inventions in this international application, as follows:	
see additional sheet	
1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.	
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.	
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:	
No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: Claims 1-7, 15-19 partially.	
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claim: 1

Invention 1:

claims 1-7, 15-19 partially

Isolated nucleotide sequence encoding an olfactory receptor as characterized by SEQID1; the recombinant expression of the same in host cells; the translated polypeptide sequence of SEQID1 and a host cell and phage expressing said polypeptide; furthermore, a library of olfactory receptors suitable of determining the interaction pattern of a composition with said receptors comprising the translated expression products of at least two, 50, 100, 200 or 500 polynucleotides encoding olfactory receptors, one of which is characterized by SEQID1.

2. Claim: 2

Invention 2-115:

claims 1-7, 15-19 partially

As invention one but as characterized by SEQIDs 2-73 and 111-152.

3. Claim: 3

Invention 116-1047:

claims 8-10 and 15-19 partially, 31,32,33 completely

Isolated nucleotide sequence encoding an olfactory receptor as characterized by one of the SEQIDs from the group of SEQID153 to SEQID1084; the recombinant expression of the same in a host cell;

furthermore, a library of olfactory receptors suitable of determining the interaction pattern of a composition with said receptors comprising the translated expression products of at least two, 50, 100, 200 or 500 polynucleotides encoding olfactory receptors, one of which is characterized by one of the SEQIDs from the group of SEQID153 to SEQID1084;

furthermore, a DNA array or a DNA chip comprising a DNA segment derived from one SEQID of the group of SEID153 to SEQID1084, a method determining the differences among individuals with respect to their olfactory faculties,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

comprising comparing the olfactory DNA of the individual against said DNA array or chip; method to determine a single nucleotide polymorphism in olfactory receptors based on primers designed according to the first and last 25 bases of one of the SEQIDs of the group of SEQID153 to SEQId1084.

4. Claim: 4

Invention 1048-1971:

claims 11-14,20-24,25-30 partially

Isolated olfactory receptor polypeptide as characterized by one of the SEQIDs from the group of SEQID1085 to SEQID2008; a recombinant host cell or phage expressing said polypeptide; furthermore, a library of olfactory receptors suitable of determining the interaction pattern of a composition with said receptors comprising at least two, 50, 100, 200 or 500 olfactory receptor polypeptides, one of which is characterized by one of the SEQIDs from the group of SEQID1085 to SEQID2008; furthermore, a method for determining the binding pattern of a composition with olfactory receptors, comprising exposing said library to a composition, further determining whether the receptor is activated.

nformation on patent family members

Interioral Application No
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Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9518140	A	06-07-1995	WO	9518140 A1	06-07-1995
WO 9850081	Α	12-11-1998	US AU EP US WO	5993778 A 7372898 A 0983506 A2 6218358 B1 9850081 A2	30-11-1999 27-11-1998 08-03-2000 17-04-2001 12-11-1998